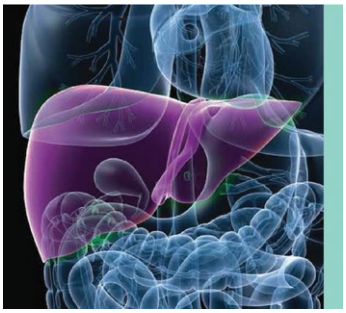

Epidemiology of Hepatitis B Virus Infection in the United States

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Hepatitis B virus (HBV) infection is one of the major public health problems worldwide. Approximately 257 million people have chronic HBV infection, which resulted in 887,000 deaths in 2015 (Fig. 1).[1,2] Global hepatitis B surface antigen (HBsAg) seroprevalence was estimated to be 3.6%, with the highest endemicity in African and Western Pacific regions (8.8% and 5.3%, respectively).[3] HBV endemicity is categorized as low (<2%), low-intermediate (2%-4.9%), high-intermediate (5%-7.9%), and high (≥8%).[4] The United States is regarded as a country with low prevalence.

In the recent decades, the HBV prevalence map has been changing as a result of systematic vaccination programs. The best example is Taiwan, which implemented active (HBV vaccine for all newborns) and passive (hepatitis B immune globulins in babies born to HBV-carrying mothers) immunization programs in the mid-1980. Thirty years later, Taiwan's HBV prevalence decreased remarkably, as shown in Fig. 2.[5] The reduction in HBV infection has been linked to a significant decrease in diseases associated with HBV infection, including hepatocellular carcinoma (HCC).

NATURAL HISTORY

HBV causes both acute and chronic infections, and is primarily transmitted through percutaneous or mucosal exposures to infected blood or body fluids. In endemic settings, perinatal transmission is the main route of infection, whereas sexual transmission, including homosexual intercourse in men, is the main route in low endemic areas. Parenteral transmission is another important mode of transmission, particularly in areas where injection drug use is common.

The risk for development of chronic hepatitis B after acute HBV infection is age dependent (Fig. 3).[6] Approximately 90% of infants become chronically infected, whereas only

Abbreviations: HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; NHANES, National Health and Nutrition Examination Survey.

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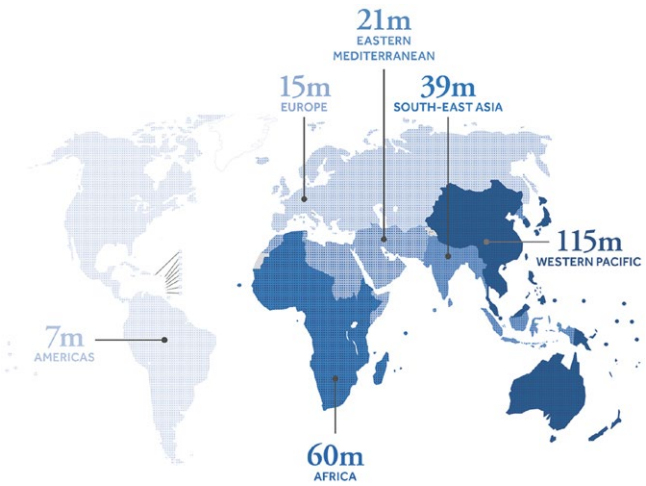

FIG 1 Global prevalence of HBV infection.

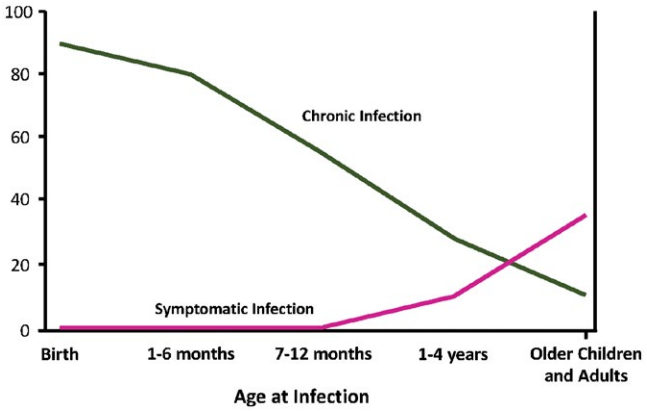

FIG 3 Age at HBV transmission and chronicity of infection.

less than 5% of adults experience chronic infection.[7] If HBV transmission occurs at age ≤5 years, long-term consequences such as chronic hepatitis, cirrhosis, or HCC would be the major problems. If the transmission occurs during adulthood, the disease burden would be primarily to manage acute infections, such as fulminant hepatitis. Approximately 1% of acute HBV infections progress to acute hepatic failure.[8] Among the 53,312 liver transplantations performed between 1993 and 2004, 0.9% was associated with HBV-related acute hepatic failure in the United States.[9]

Once chronic infection is established, cirrhosis occurred at an annual rate of 2% to 5% and 8% to 10% in hepatitis B e antigen (HBeAg)-positive and HBeAg-negative patients, respectively.[10] Approximately 3% of patients with cirrhosis develop decompensation annually.[10] The risk for HCC is 2% to 3% per year in patients with cirrhosis and less than 1% per year in those without.[7] HBV accounts for 10% to 15% of HCC cases in the United States.[11]

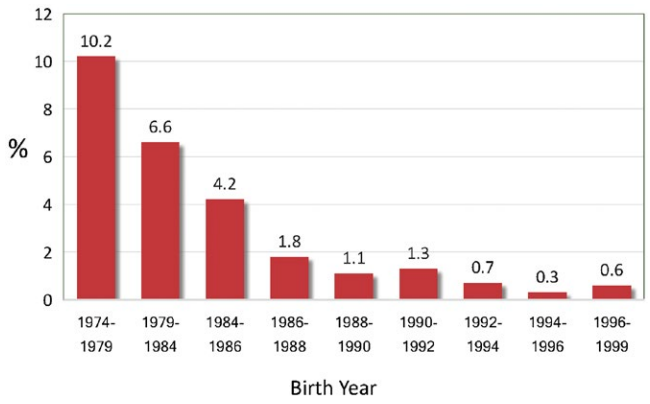

FIG 2 Prevalence of HBsAg+ in Taiwan.

INCIDENCE OF ACUTE HBV INFECTION

HBV infection is preventable by vaccination. The incidence of new HBV infection decreased dramatically in the early 1990s after mandatory screening of pregnant women with HBsAg and universal vaccination of the newborns. The peak incidence of reported acute HBV infection was 11.5 per 100,000 in 1985, which went down by nearly 4-fold to 2.9 by 2000.[12]

Figure 4 summarizes more recent data on acute HBV infection.[13] Between 2000 and 2012, the downward trend continued for all age groups. The age group that showed the most consistent reduction in HBV incidence was children and adults in their 20s, the generation that received HBV vaccine as infants.[13] In contrast, in other age groups, namely the 30- to 49-year-olds, the HBV incidence curves have turned back up. Similarly, the incidence rates among the American Indian/Alaska natives, non-Hispanic blacks, Asian/Pacific Islander, and Hispanics decreased in 2000 to 2015, whereas the rate among non-Hispanic whites slightly increased in 2009 to 2015.[13]

Figure 5 provides another snapshot of the increasing incidence of HBV infection.[14] The data show that there has been a dramatic increase in HBV incidence in the three

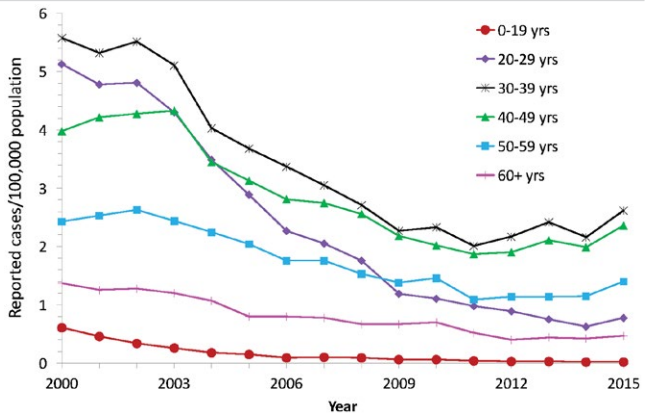

FIG 4 Incidence of acute hepatitis B in the United States (2005-2015).

states in the Appalachian region, particularly in the nonurban area. Identified cases consistently reported injection drug use, revealing HBV transmission represents another consequence of the resurgent epidemic of injection drug use. It is worrisome that the trend shown in Fig. 5 is likely to have continued in more recent years.[15]

PREVALENCE OF CHRONIC HBV INFECTION

The estimated prevalence of chronic HBV infection is 847,000 persons (0.3%) according to the recent National Health and Nutrition Examination Survey (NHANES) between 2011 and 2012. It has remained steady since 1988 (0.4% during 1988-1994 and 0.3% during 1999-2006). However, these prevalence data are understood to be a significant underestimation because NHANES did not include appropriate samples of population groups with the highest prevalence of HBV, namely Native Americans, Alaskan Natives, Asians, and Pacific Islanders.[16] A recent NHANES study that included a larger number of non-Hispanic Asians than previously reported the prevalence rate of chronic HBV infection among Asians, non-Hispanic blacks, and non-Asian/non-blacks to be 2.74%, 0.64%, and 0.15%, respectively.[17]

Estimates of HBV infection among foreign-born US residents have been reported based on the number of immigrants from each region of the world and the estimated prevalence of HBV infection in the originating countries (Fig. 6).[16] The best estimate for foreign-born persons with chronic HBV infection was 1.32 million (1.04 million-1.61 million), which included approximately 730,000 from Asia.[18] It also included approximately 310,000 subjects of African Ancestry coming from Africa or the Caribbean. Even though HBV is commonly thought of as an Asian disease, it is important to highlight that immigrants of African descent should also be screened for HBV infection.

Another part of the population that NHANES excludes is institutionalized, homeless, or incarcerated people, all of whom are expected to have higher probabilities of HBV infection. All in all, a recent Centers for Disease Control and Prevention publication estimates the total prevalence of chronic HBV infection in the United States at 2.2 million, including noninstitutionalized US-born persons, foreign-born immigrants with existing HBV infection, and institutionalized individuals (n = ~74,000).[19]

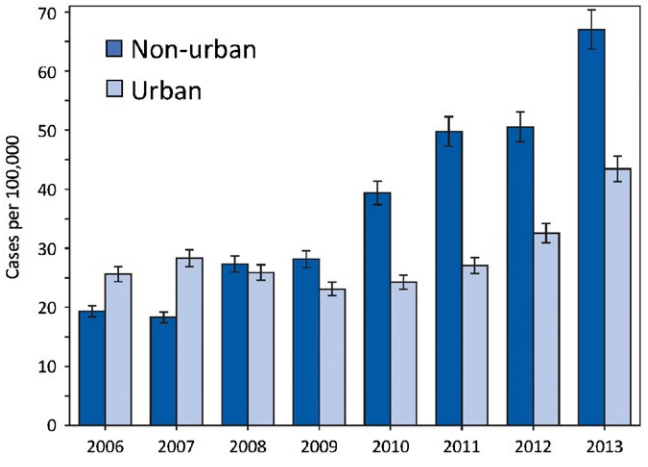

FIG 5 Incidence of acute hepatitis B in Kentucky, Tennessee, and West Virginia.

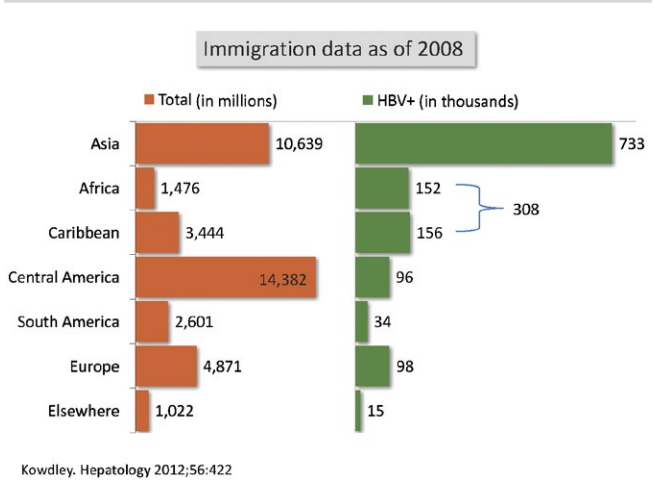

FIG 6 HBV infection prevalence in foreign-born US residents.[18]

CONCLUSION

HBV is an important cause of acute and chronic liver disease in the United States. A successful vaccination program has been implemented over the last two decades, thereby decreasing the number of new cases of HBV infection. However, the estimated prevalence rate of the general population still remains at 0.3% and has even been underestimated. Recent studies suggest imported cases should be considered and influence the actual prevalence of HBV infection. Higher prevalence increases the disease burden because HBV causes severe liver disease and HCC. Therefore, more active surveillance and careful monitoring are warranted.

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